REMARKS

Claims 4 to 8 and 24 to 29 are in the case.

Reconsideration of this Application and entry of the foregoing amendments are requested. The Examiner requires that claims 1-3 and 9-18, directed to non-elected inventions, be cancelled pursuant to 37 CFR 1.144. The Applicants have thus cancelled these claims in conformity with 37 CFR 1.144. Applicants reserve the right to prosecute the subject matter of these cancelled claims in further applications.

Claims 19 to 23 have also been cancelled. Claim 25 has been amended and claims 26 to 29 have been added in view of the Office Action and to better define what the Applicants consider their invention, as fully supported by an enabling disclosure. Claim 25 (d) has been amended and now relates to a nucleotide sequence encoding "a staufen polypeptide". Additional support for this amendment may be found in old claim 25(d). Additional support for new claims 26 to 29 may be found, for example, in old claims 20-23 to which they are identical, except for their dependencies.

The Examiner alleges that no certified copy of the Canadian application no. 2,238,656 on which foreign priority is claimed was received. For this reason, the denial of priority was maintained. Accordingly, and because our agent has apparently not kept any evidence of its filing of the priority document, a new certified copy is enclosed for the Examiner's convenience. The Applicants respectfully request reconsideration of their request for foreign priority.

The Applicants note the Examiner's conclusion that the nucleic acid sequences of SEQ ID NO: 1, 3, 5, 7 and 9 are free of the prior art of record.

REJECTION UNDER 35 U.S.C. § 112 FIRST PARAGRAPH

The Applicants note that although the Examiner considers that the specification does not enable claims presently on file, he considers that the specification would be enabling for claims covering:

"(i) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO 1, 3, 5, 7 and 9, (ii) an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO 6, SEQ ID NO 11, SEQ ID NO 2, amino acid residues 2-577 of SEQ ID NO 6 and amino acid residues 2-487 of SEQ ID NO 11; and (iii) a nucleic acid complimentary to the full length nucleic acids of (i)-(iii), a recombinant vector comprising the isolated nucleic acid, a method of making a recombinant host cell comprising the isolated nucleic acid, a host comprising the nucleic acid, and a method of making the polypeptide encoded by the nucleic acid."

The Examiner therefore appears to indicate that if the claims were reworded accordingly, they would presumably be allowable (see section 9, at p. 3 first par.; and at pages 6 and 7, last and first paragraph, respectively). The Applicants believe however that they are entitled to the pending claims as explained below.

REJECTION UNDER 35 U.S.C. § 112 FIRST PARAGRAPH

The Examiner rejects claims 4-8 and 19-25 under 35 U.S.C. 112, first paragraph on various grounds detailed below under separate headings.

REJECTION ON THE BASIS THAT CURRENT CLAIMS COULD ALLEGEDLY COVER POLYNUCLEOTIDES THAT DO NOT ENCODE STAUFEN

The Examiner first indicates that the specification is not enabling for a "nucleic acid encoding a Staufen polypeptide comprising amino acids 82-577 or 83-577 of SEQ ID NO: 6 or other recited embodiments". Although it is not specified, the Applicants understand this objection to relate to the wording of claims 4(b) and (d).

The Examiner's objection seems to result from a misunderstanding of the relation between the amino acid sequence in SEQ ID NO: 6 and the sequence appearing in Fig 1b. According to the Examiner's understanding, the RNA binding domains ("RBD") of the protein, namely RBD1 to RBD4, are located, according to Figure 1b, at the N-terminus upstream of aa 39, between aa 62 and 128, in the middle of the protein, and in the C-terminus of the protein, respectively. The Examiner therefore understands that a protein containing 82-577 or 83-577 of SEQ ID NO: 6 would lack

RBD1 and a portion of RBD2. He therefore alleges that it is not clear whether these fragments would bind to dsRNA or would have any other activity attributed to full length SEQ ID NO: 6 or, in other words, whether they would have the function of the protein of SEQ ID NO: 6. The Applicant wishes to point out to the Examiner that: 1) the localization of the domains are indicated **above** the sequence in fig. 1b (*and not below as the Examiner seems to have understood.* Thus, these domains are actually located between amino-acids 59-79, 102-168, 205-271 and 452-472 in fig. 1b; and 2) the first amino acid of SEQ ID NO: 6 corresponds to the amino acid number –81 of fig. 1b (*and not to amino acid no. 1 as the Examiner appears to understand*) and its last amino acid corresponds to the amino acid number 496 of fig. 1b.

It should thus become apparent to the Examiner that the sequences of amino acids recited in claim 4(b) and (d), namely from 82 to 577 and from 83 to 577 of SEQ ID NO: 6, respectively, correspond to the amino acids sequences from 1 to 496, and 2 to 496 in fig. 1b, respectively. Each of these sequences therefore contains all four RBDs appearing in fig. 1b. For additional clarity, the sequences of amino acids recited in claim 4(e) and (f), namely from 1 to 487 and 2 to 487 of SEQ ID NO: 11, respectively, correspond to the sequences of amino acids from 1 to 487, and 2 to 487 of fig. 1c, respectively. In the same manner, the amino acids sequence recited in claim 4(g), namely the amino acid sequence of SEQ ID NO: 27, corresponds to the amino acid sequence of *C. elegans* appearing in fig. 1' in the alignment for CEL. Finally, the amino acids sequence recited in claim 4(h), namely the amino acid sequence of SEQ ID NO: 2, corresponds to the human amino acid sequence encoded by the sequence of nucleotides designated SEQ ID NO: 1.

In view of this clarification, it is believed that the rejection of claim 4 under USC §112 first paragraph should be withdrawn.

The Examiner then rejects claim 19 as containing subject matter that was allegedly not described in the specification in such a way as to convey that the inventors had possession of the invention claimed. Claim 19 recites a sequence that is 95% identical to SEQ ID NO: 1, 3, 5 or 7, any sequence that is complementary to these

sequences or a sequence that hybridizes to these sequences. The Examiner notes that because this claim covers any sequence that is complementary or that may hybridize to these sequences, this claim may encompass nucleic acid molecules that do not encode Staufen, for instance the 385bp sequence disclosed in Banfi. The Applicants submit that this rejection is rendered moot by the cancellation of claim 19. The Applicants therefore respectfully request that this objection under USC §112 first paragraph be withdrawn.

REJECTION BASED ON THE USE OF WORDING "95% IDENTICAL"

The Examiner then objects to the wording "95 % identical" in claims 4, 19, 24 and 25. The Applicants first wish to point out that they assume that the Examiner's objection to claim 25 on this basis was a mistake since this claim does not include the objected wording. The Applicants also submit that claim 19 was cancelled. The Examiner maintains his opinion that since the disclosure does not teach which 5% of the recited nucleotides could be substituted without altering the activity of the encoded protein, it is not enabling for such wording. The Applicants respectfully disagree as follows.

The Examiner is respectfully referred to Example 14 of the Synopsis of Application of Written Description Guidelines published by the USPTO (the "Guidelines"). This Example relates to a product by function claim reciting a protein having a specific sequence or variants that are at least 95% identical to this specific sequence and have a specific function. In the analysis of this claim, the USPTO concludes that this claim would meet the requirement of 35 USC 112, first paragraph as providing adequate sufficient description. The USPTO bases its conclusion on the following elements: 1) an assay is described which will identify other proteins having the claimed activity; 2) procedures for making variants of the specific sequence having 95 % identity and retaining their activity are conventional in the art; 3) the genus of proteins claimed do not have a substantial variation since they all possess the recited activity and they must have at least 95% identity with the claimed sequence; and 4) the species disclosed is representative of the genus because all members have at least 95% structural identity with the reference protein.

The Applicants submit that claims 4 and 24 therefore meet the requirement of 35 USC 112, first paragraph because the instant specification comprises all the above elements: 1) an assay is described which will identify other nucleic acid molecules which encode Staufen. Examples 11 and 12 of the instant application show how human and mouse staufen were tested to determine whether they bind to double-stranded RNAs and to tubulin. These examples indicate that fusion proteins expressing the Staufens were probed with *in-vitro* labeled bicoid mRNA and tubulin. A person of ordinary skill in the art could therefore use these assays to determine whether sequences having 95% identity with the claimed sequences have these staufen activities; 2) procedures for making variants of the specific sequence having 95 % identity and retaining their activity are conventional in the art. The herein disclosed alignments of Staufen go even further since they can be used as starting points to identify and characterize amino acids which can or cannot withstand modifications; 3) the genus of proteins claimed do not have a substantial variation since they all possess the recited activity and they must have at least 95% identity with the claimed sequence. The Applicant submits that the claimed nucleic acid molecules satisfy this requirement; and 4) the species disclosed is representative of the genus because all members have at least 95% structural identity with the reference protein. The Applicant submits that the claimed nucleic acid molecules satisfy this requirement.

The Applicants therefore respectfully request that the Examiner withdraws his rejection of claims 4, 19, 24 (and 25) under 35 USC §112 first paragraph.

REJECTION BECAUSE OF THE WORDING "ENCODING CONSERVATIVE SUBSTITUTION"

The Examiner then rejects claim 25 d) because it "recites a nucleotide sequence encoding conservative substitution of the sequence of 25 a, b and c". The Applicant submits that in view of the newly amended claim 25(d) which recites a nucleotide sequence encoding a staufen polypeptide, this rejection should be withdrawn. The Applicants submit that the argument presented above as to the sufficiency of the instant disclosure for claims reciting a nucleotide sequence that is 95% identical to a recited sequence and that has a specific function equally apply here. Procedures for

determining which nucleotide may be modified without changing the staufen function are conventional in the art. In addition, fig. 1d shows an alignment of the mouse and human staufen highlighting the conservative substitution in the protein. In this alignment, conservative changes are emphasized by single dots. This figure may therefore also guide the skilled reader as to which nucleotides may be substituted without affecting the staufen activity of the protein. The Applicants therefore respectfully request that the Examiner withdraws his rejection of claim 25 under 35 USC §112 first paragraph.

REJECTION BASED ON LACK OF SUFFICIENT DESCRIPTION OF SEQUENCES ENCOMPASSED IN CLAIM 19 (E) AND (F)

The Examiner rejected claim 19 e) and f) reciting sequences complementary to or hybridizing with sequences identified in 19 (a) to (d) because those sequences have not been sufficiently described by other relevant identifying characteristics, features and attributes.

The Applicants submit that this objection is rendered moot in view of the cancellation of claim 19 and therefore respectfully request that this objection under 35 USC §112 first paragraph be withdrawn.

NEW MATTER REJECTION

The Examiner remains of the opinion that claim 4 contains subject matter which was not described in the specification. The Applicants wish to point out to the Examiner that the number "27" appearing in the instant sequence listing beside the symbols <210> and <400> refers to the number of the sequence while that appearing beside the symbol <211> refers to the number of amino acid contained in the sequence, namely, for SEQ ID NO: 27, 705 amino acids. The Applicants therefore respectfully submit that SEQ ID NO: 27 is not a 27 amino acid polypeptide but a 705 amino acid sequence which is identical to the 705 amino acid sequence disclosed on fig. 1' and 1'(cont'd).

Accordingly, the Applicants therefore respectfully request that the new matter rejection of claim 4 under 35 USC §112 first paragraph be withdrawn.

REJECTION UNDER 35 U.S.C. § 112 SECOND PARAGRAPH

The Examiner remains of the opinion that claim 19 is indefinite because it recites the term "highly stringent conditions". The Examiner alleges that this term is relative and "what might be considered high stringent in one situation may not be stringent in another situation". The Applicants submit that this objection is rendered moot in view of the cancellation of claim 19 and therefore respectfully request that this objection under 35 USC §112 second paragraph be withdrawn.

The Applicants wish to point out that claim 24 still contains this terminology. The Applicants however submit that this wording does not render claim 24 indefinite for the following reasons.

The Examiner is respectfully referred to Example 9 of the Guidelines, which relates to an isolated nucleic acid defined by 1) its ability to hybridize with a known sequence; and 2) its function. In the Example, the wording used to define hybridization conditions is "highly stringent conditions". The USPTO therefore recognizes that this wording refers to conditions that are conventional in the art. Furthermore, although these conditions vary according to the nature of the sequence, they are easily determined by a person of ordinary skill in the art which may simply look into prior art charts indicating the parameters of highly stringent conditions for any sequence depending on its content in guanine and cytosine. In addition, examples of "highly stringent conditions" are given in the instant disclosure (for example at page 23, lines 18-21).

The Examiner points out typographical errors in claim 19. The Applicants submit that this objection is rendered moot in view of the cancellation of claim 19 and therefore respectfully request that this objection be withdrawn.

REJECTION UNDER 35 USC § 102 (b)

The Examiner remains of the opinion that claim 19 is anticipated by Marra et al. The argument according to which Marra's sequence is in the untranslated region and therefore is not encompassed by the claimed invention was deemed unpersuasive because claim 19 is not so limited.

The Applicants submit that this objection is rendered moot in view of the cancellation of claim 19 and therefore respectfully request that the rejection pursuant to 102 (b) be withdrawn.

REJECTION UNDER 35 USC § 102 (a)

The Examiner remains of opinion that claim 19 is anticipated by Banfi. The Examiner alleges that the Nature Genetics article indicates that Banfi used clone #22363 for amplifying the cited sequence and taught that the 5' end of that clone has homology to the Staufen gene of *Drosophilya*. The Examiner therefore concludes that it is clear that the sequence in the accession number was known at the time of the publication of the article in Nature Genetics. The Applicants respectfully disagree as follows.

The sequence allegedly known by Banfi at the crucial date, has a 99.2% similarity, according to the Examiner at page 5 of his Office Action, with nt 2705-3089 of SEQ ID NO: 1, with nt 3069-3453 of SEQ ID NO: 5 and with nt 2911-3295 of SEQ ID NO: 7. The Banfi sequence is therefore in an untranslated region of the claimed sequence as is apparent in the relevant portions of SEQ ID NOS: 1, 5 and 7, respectively (hence they do not encode a *Staufen* polypeptide).

In any event, the Applicants submit that this objection is rendered moot in view of the cancellation of claim 19 and therefore respectfully request that the rejection pursuant to 102(a) be withdrawn.

CONCLUSION

The rejections of the original claims are believed to have been overcome by the present remarks and the introduction of new claims. From the foregoing, further and

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 25 has been amended as follows: Underlines indicate insertions.

25. (Amended) An isolated nucleic acid molecule comprising a polynucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a *staufen* polypeptide comprising amino acids 1 to 591 of SEQ ID NO:2;

(b) a nucleotide sequence encoding a *staufen* polypeptide comprising amino acids 1 to 577 of SEQ ID NO:6;

(c) a nucleotide sequence encoding a *staufen* polypeptide comprising amino acids 2 to 577 of SEQ ID NO:6; and

(d) a nucleotide sequence encoding a *staufen* polypeptide and conservative substitutions of the polypeptides encoded by any of the sequences in (a), (b) or (c).

favorable action in the form of a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited.

It should be understood that claim amendments for which no explanation is established above were made for clarity purposes only and not for reasons related to statutory requirements for patentability.

Authorization is hereby given to charge deposit account no. 07-1742 for any deficiencies or overages in connection with this response.

Respectfully submitted,

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Reg. No. 48,089

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Encls.: Certified copy of Canadian application no. 2,238,656